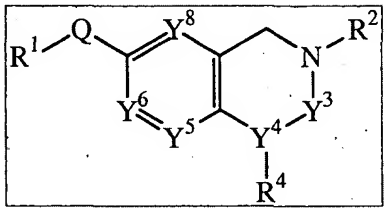
CLAIMS

What is claimed is:

1. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof,

wherein:

R^1 is independently selected from:

C_5 or C_6 cycloalkyl-(C_1-C_8 alkylenyl);

Substituted C_5 or C_6 cycloalkyl-(C_1-C_8 alkylenyl);

C_8-C_{10} bicycloalkyl-(C_1-C_8 alkylenyl);

Substituted C_8-C_{10} bicycloalkyl-(C_1-C_8 alkylenyl);

5- or 6-membered heterocycloalkyl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heterocycloalkyl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobicycloalkyl-(C_1-C_8 alkylenyl);

Substituted 8- to 10-membered heterobicycloalkyl-(C_1-C_8 alkylenyl);

Phenyl-(C_1-C_8 alkylenyl);

Substituted phenyl-(C_1-C_8 alkylenyl);

Naphthyl-(C_1-C_8 alkylenyl);

Substituted naphthyl-(C_1-C_8 alkylenyl);

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Phenyl;

Substituted phenyl;

Naphthyl;

Substituted naphthyl;

5- or 6-membered heteroaryl;

Substituted 5- or 6-membered heteroaryl;

8- to 10-membered heterobiaryl; and

Substituted 8- to 10-membered heterobiaryl;

R^2 is independently selected from:

H;

C_1-C_6 alkyl;

Phenyl-(C_1-C_8 alkylenyl);

Substituted phenyl-(C_1-C_8 alkylenyl);

Naphthyl-(C_1-C_8 alkylenyl);

Substituted naphthyl-(C_1-C_8 alkylenyl);

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl);

Phenyl-O-(C_1-C_8 alkylenyl);

Substituted phenyl-O-(C_1-C_8 alkylenyl);

Phenyl-S-(C_1-C_8 alkylenyl);

Substituted phenyl-S-(C_1-C_8 alkylenyl);

Phenyl-S(O)-(C_1-C_8 alkylenyl);

Substituted phenyl-S(O)-(C_1-C_8 alkylenyl);

Phenyl-$S(O)_2$-(C_1-C_8 alkylenyl); and

Substituted phenyl-$S(O)_2$-(C_1-C_8 alkylenyl);

Each substituted R^1 and R^2 group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

C_1-C_6 alkyl;

CN;

CF_3;

HO;

(C_1-C_6 alkyl)-O;

(C_1-C_6 alkyl)-$S(O)_2$;

H_2N;

(C_1-C_6 alkyl)-N(H);

$(C_1\text{-}C_6$ alkyl$)_2$-N;

$(C_1\text{-}C_6$ alkyl$)$-C(O)O-$(C_1\text{-}C_8$ alkylenyl$)_m$;

$(C_1\text{-}C_6$ alkyl$)$-C(O)O-(1- to 8-membered heteroalkylenyl$)_m$;

$(C_1\text{-}C_6$ alkyl$)$-C(O)N(H)-$(C_1\text{-}C_8$ alkylenyl$)_m$;

$(C_1\text{-}C_6$ alkyl$)$-C(O)N(H)-(1- to 8-membered heteroalkylenyl$)_m$;

$H_2NS(O)_2$-$(C_1\text{-}C_8$ alkylenyl$)$;

$(C_1\text{-}C_6$ alkyl$)$-N(H)S$(O)_2$-$(C_1\text{-}C_8$ alkylenyl$)_m$;

$(C_1\text{-}C_6$ alkyl$)_2$-NS$(O)_2$-$(C_1\text{-}C_8$ alkylenyl$)_m$;

3- to 6-membered heterocycloalkyl-$(G)_m$;

Substituted 3- to 6-membered heterocycloalkyl-$(G)_m$;

5- or 6-membered heteroaryl-$(G)_m$;

Substituted 5- or 6-membered heteroaryl-$(G)_m$;

$(C_1\text{-}C_6$ alkyl$)$-S$(O)_2$-N(H)-C(O)-$(C_1\text{-}C_8$ alkylenyl$)_m$; and

$(C_1\text{-}C_6$ alkyl$)$-C(O)-N(H)-S$(O)_2$-$(C_1\text{-}C_8$ alkylenyl$)_m$;

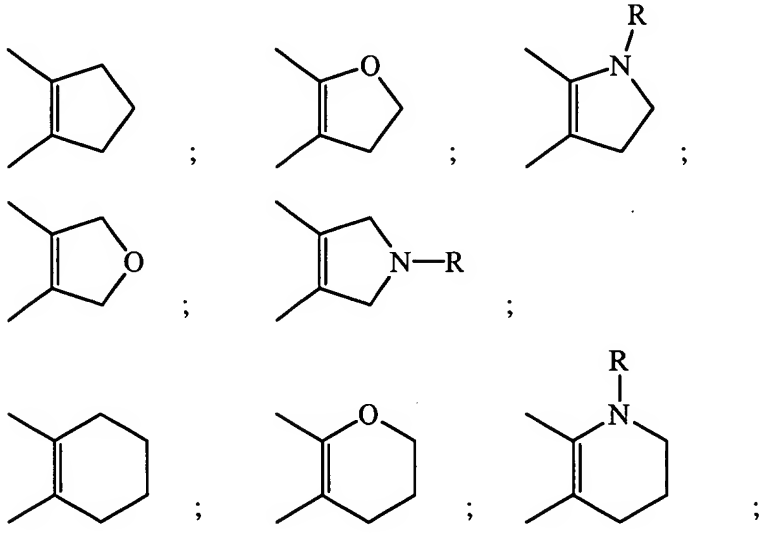
wherein each substituent on a carbon atom may further be independently selected from:

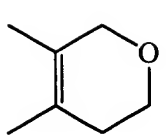
Halo; and

HO_2C;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

wherein two adjacent, substantially sp^2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:

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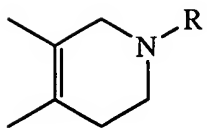
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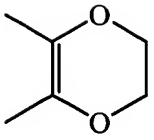
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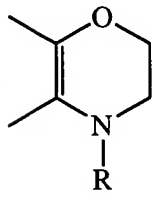
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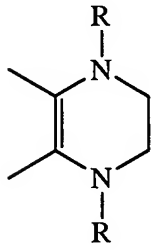
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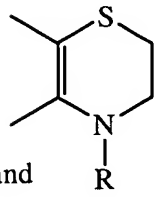
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R is H or C_1-C_6 alkyl;

G is CH_2; O, S, S(O); or $S(O)_2$;

m is an integer of 0 or 1;

Y^4, Y^5, Y^6, and Y^8 are each independently $C(R^5)$ or N;

Y^3 is C(O) or CH_2;

R^4 and each R^5 are each independently selected from the groups:

H;

CH_3;

CH_3O;

$CH=CH_2$;

HO;

CF_3;

CN;

HC(O);

$CH_3C(O)$;

HC(NOH);

H_2N;

(CH_3)-N(H);

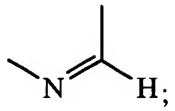
$(CH_3)_2$-N;

$H_2NC(O)$;

(CH_3)-N(H)C(O); and

$(CH_3)_2$-NC(O); or

R^4 and Y^3 may be taken together to form a diradical group:



Q is selected from:

OC(O);

$CH(R^6)C(O)$;

$OC(NR^6)$;

$CH(R^6)C(NR^6)$;

$N(R^6)C(O)$;

$N(R^6)C(S)$;

$N(R^6)C(NR^6)$;

$N(R^6)CH_2$;

SC(O);

$CH(R^6)C(S)$;

$SC(NR^6)$;

trans-(H)C=C(H);

cis-(H)C=C(H);

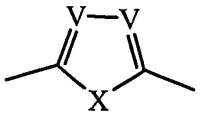
C≡C;

$CH_2C{\equiv}C$;

$C{\equiv}CCH_2$;

$CF_2C{\equiv}C$; and

$C{\equiv}CCF_2$;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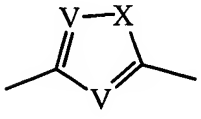
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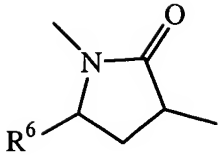
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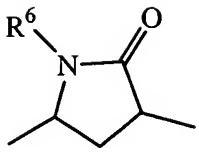
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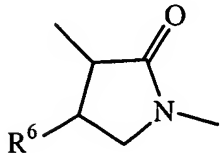
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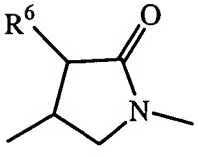
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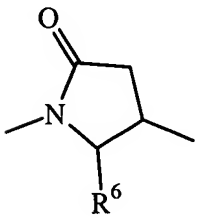
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Each R^6 independently is H, C_1-C_6 alkyl, C_3-C_6 cycloalkyl; 3- to 6-membered heterocycloalkyl; phenyl; benzyl; or 5- or 6-membered heteroaryl;

X is O, S, N(H), or N(C_1-C_6 alkyl);

Each V is independently C(H) or N;

wherein each C_8-C_{10} bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;

wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 4 N(H), and 4 N(C_1-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 $S(O)_2$, 1 N, 4 N(H), and 4 N(C_1-C_6 alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C_1-C_6 alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C_1-C_6 alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O

and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any $(C_1\text{-}C_6$ alkyl$)_2$-N group, the $C_1\text{-}C_6$ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

wherein each group and each substituent recited above is independently selected.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Y^5, Y^6, and Y^8 are each $C(R^5)$, wherein each R^5 is independently defined as above.

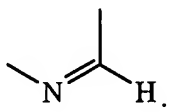
3. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein one of Y^5, Y^6, and Y^8 is N and the other two of Y^5, Y^6, and Y^8 are each $C(R^5)$, wherein each R^5 is independently defined as above.

4. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is $N(R^6)C(O)$.

5. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is C≡C.

6. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Y^3 is C(O).

7. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Y^3 and R^4 is taken together to form a diradical group:



8. The compound according to any one of Claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein R^1 is independently selected from:

Phenyl-(C_1-C_8 alkylenyl);

Substituted phenyl-(C_1-C_8 alkylenyl);

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl);

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl); and

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl); and

R^2 is independently selected from:

Phenyl-(C_1-C_8 alkylenyl)$_m$;

Substituted phenyl-(C_1-C_8 alkylenyl)$_m$;

5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl)$_m$;

Substituted 5- or 6-membered heteroaryl-(C_1-C_8 alkylenyl)$_m$;

8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl)$_m$; and

Substituted 8- to 10-membered heterobiaryl-(C_1-C_8 alkylenyl)$_m$;

wherein m is an integer of 0 or 1; and

wherein each group and each substituent is independently selected.

9. The compound according to Claim 1, selected from:

3-(4-Methanesulfonyl-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-quinazoline-6-carboxylic acid (pyridin-4-ylmethyl)-amide;

3-(4-Methanesulfonyl-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-quinazoline-6-carboxylic acid (pirimidin-5-ylmethyl)-amide;

3-(4-Methanesulfonyl-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-quinazoline-6-carboxylic acid 4-methoxy-benzylamide;

3-(3-Chloro-4-fluoro-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-quinazoline-6-carboxylic acid 4-methoxy-benzylamide;

4-[6-(4-Methoxy-benzylcarbamoyl)-1-methyl-2-oxo-1,4-dihydro-2H-quinazolin-3-ylmethyl]-benzoic acid;

3-(4-Bromo-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-quinazoline-6-carboxylic acid (pyridin-4-ylmethyl)-amide;

1-Methyl-3-(4-methylsulfanyl-benzyl)-2-oxo-1,2,3,4-tetrahydro-quinazoline-6-carboxylic acid 3-methoxy-benzylamide;

3-(4-Methanesulfonyl-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-pyrido[3,4-d]pyrimidine-6-carboxylic acid (pyridin-4-ylmethyl)-amide;

3-(3-Chloro-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-pyrido[3,4-d]pyrimidine-6-carboxylic acid (2-methoxy-pyridin-4-ylmethyl)-amide;

3-(4-Cyano-benzyl)-1-methyl-2-oxo-1,2,3,4-tetrahydro-pyrido[3,4-d]pyrimidine-6-carboxylic acid (pyridin-4ylmethyl)-amide;

4-[6-(4-Methoxy-benzylcarbamoyl)-1-methyl-2-oxo-1,4-dihydro-2H-pyrido[3,4-d]pyrimidin-3-ylmethyl]-benzoic acid;

4-[6-(4-Methoxy-benzylcarbamoyl)-methyl-2-oxo-1,4-dihydro-2H-pyrido[2,3-d]pyrimidin-3-ylmethyl]-benzoic acid;

1-Methyl-3-(4-methylsulfanyl-benzyl)-2-oxo-1,2,3,4-tetrahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid (pyridin-3-ylmethyl)-amide;

3-(4-Isopropyl-benzyl)-methyl-2-oxo-1,2,3,4-tetrahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid (pyrimidin-5-ylmethyl)-amide;

1-Methyl-3-pyridin-3-ylmethyl-1,2,3,4-tetrahydro-quinazoline-6-carboxylic acid 4-methyl-benzylamide;

{4-[6-Methoxy-benzylcarbamoyl)-1-methyl-1,4-dihydro-2H-pyrido[3,4-d]pyrimidin-3-ylmethyl]-phenyl}-acetic acid;

3-Benzyl-1-methyl-1,2,3,4-tetrahydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid benzylamide;

3-Benzyl-3,4-dihydro-quinazoline-6-carboxylic acid 4-chloro-benzylamide;

3-Benzyl-3,4-dihydro-pyrido[3,4-d]pyrimidine-6-carboxylic acid (benzo[1,3]dioxo-5-ylmethyl)-amide; and

3-Benzyl-3,4-dihydro-pyrido[2,3-d]pyrimidine-6-carboxylic acid 3-fluoro-benzylamide;

or a pharmaceutically acceptable salt thereof.

10. The compound according to Claim 1, selected from:

3-(4-Methanesulfonyl-benzyl)-1-methyl-6-(3-phenyl-prop-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;

6-(3-Imidazol-1-yl-prop-1-ynyl)-3-(4-methanesulfonyl-benzyl)-1-methyl-3,4-dihydro-1H-quinazolin-2-one;

6-[3-(4-Fluoro-phenyl)-prop-1-ynyl]-3-(4-methanesulfonyl-benzyl)-1-methyl-3,4-dihydro-1H-quinazolin-2-one;

6-[3-(4-Chloro-phenyl)-prop-1-ynyl]-3-(4-methanesulfonyl-benzyl)-1-methyl-3,4-dihydro-1H-quinazolin-2-one;

3-(4-Methanesulfonyl-benzyl)-1-methyl-6-(3-pyridin-4-yl-prop-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;

3-(4-Methanesulfonyl-benzyl)-1-methyl-6-(4-phenyl-but-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;

3-(4-Methanesulfonyl-benzyl)-1-methyl-6-(3-naphthalen-2-yl-prop-1-ynyl)-3,4-1H-quinazolin-2-one;

3-Benzyl-1-methyl-6-(3-phenyl-prop-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;

4-[1-Methyl-2-oxo-6-(3-phenyl-prop-1-ynyl)-1,4-dihydro-2H-quinazolin-3-ylmethyl]-benzoic acid;

3-(4-Chloro-benzyl)-1-methyl-6-(3-phenyl-prop-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;

3-(3,4-Difluoro-benzyl)-methyl-6-(3-phenyl-prop-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;

3-(4-Methoxy-benzyl)-1-methyl-6-(3-phenyl-prop-1-ynyl)-3,4-dihydro-1H-quinazolin-2-one;

4-[1-Methyl-2-oxo-6-(3-phenyl-prop-1-ynyl)1,4-dihydro-2H-quinazolin-3-ylmethyl]-benzonitrile;

5-[1-Methyl-2-oxo-6-(3-phenyl-prop-1-ynyl)-1,4-dihydro-2H-quinazolin-3-ylmethyl]furan-2-carboxylic acid;

4-[1-Methyl-6-(3-methyl-3-phenyl-but-1-ynyl)-2-oxo-1,4-dihydro-2H-pyrido[2,3-d]pyrimidin-3-ylmethyl]benzoic acid;

3-Benzyl-1-methyl-6-(3-phenyl-prop-1-ynyl)-1,2,3,4-tetrahydro-pyrido[2,3-d]pyrimidine;

3-[6-(3-Phenyl-prop-1-ynyl)-4H-pyrido[2,3-d]pyrimidin-3-ylmethyl]benzonitrile; and

4-[6-(3,3-Difluoro-3-phenyl-prop-1-ynyl)-4H-quinazolin-3-ylmethyl]-benzoic acid;

or a pharmaceutically acceptable salt thereof.

11. A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

12. The pharmaceutical composition according to Claim 11, comprising a compound according to Claim 9 or 10, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

13. A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis or rheumatoid arthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

14. The method according to Claim 11, wherein the compound administered is a compound according to Claim 9 or 10, or a pharmaceutically acceptable salt thereof.